Case Report

Large Scrotal Verruciform Xanthoma (VEGAS Xanthoma): A Case Report

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Abstract

Background: Verruciform xanthoma is a rare benign lesion most commonly involving oral mucosa. Genital involvement is uncommon. Large scrotal verruciform xanthomas are particularly rare and may clinically mimic verrucous or papillomatous lesions. Chronic irritation and epithelial damage are considered possible contributing factors. **Case Presentation:** A 76-year-old male presented with a gradually enlarging scrotal mass clinically diagnosed as papilloma. Histopathological examination revealed hyperplastic squamous epithelium with papillomatosis and numerous foamy macrophages within fibrovascular cores, confirming verruciform xanthoma. **Conclusion:** The present case is noteworthy due to its relatively large size, scrotal location, and close clinical resemblance to papilloma, highlighting the indispensable role of histopathological examination in establishing the diagnosis to avoid diagnostic pitfalls and unnecessary aggressive management.

Keywords: Xanthoma, Foam cells.

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Introduction

Verruciform xanthoma is a papillary or cauliflower-like growth seen chiefly in the oral mucosa. It was first described by Shafer in 1971.[1] The reported incidence of verruciform xanthoma ranges from 0.025% to 0.05%.[1] Clinically, these lesions are often mistaken for papilloma or other verrucous lesions.

The most common extraoral verruciform xanthomas are reported in the genital region where they have recently been termed VEGAS (verruciform genital-associated) xanthomas.[2]

The exact incidence of genital verruciform xanthoma remains unknown due to its rarity, with fewer than 200 cases reported in literature. The most common age group is 40 to 70 years with a male preponderance.[1] Clinically, these lesions commonly present as slow-growing verrucous or papillomatous plaques resembling a wart with a size range of 0.5 to 2.5 cm and are often mistaken for papilloma, condyloma acuminatum, verruca vulgaris, or verrucous carcinoma. Large genital verruciform xanthomas are uncommon.

We report a case of a large 4cm scrotal verruciform xanthoma in a 76-year-old male that was clinically suspected to be papilloma.

Case Presentation

A 76-year-old male patient presented with a gradually enlarging scrotal mass for 6 months. Patient had no other significant history or comorbidities. On physical examination, the mass was 4 x 3 x 2 cm [Figure 2A]. Ultrasonography revealed a well-defined pedunculated oval shaped heterogenous lesion overlying the left scrotal region with mild internal vascularity. Findings were suggestive of benign etiology like papilloma. Surgical excision was done and specimen was sent for histopathological examination.

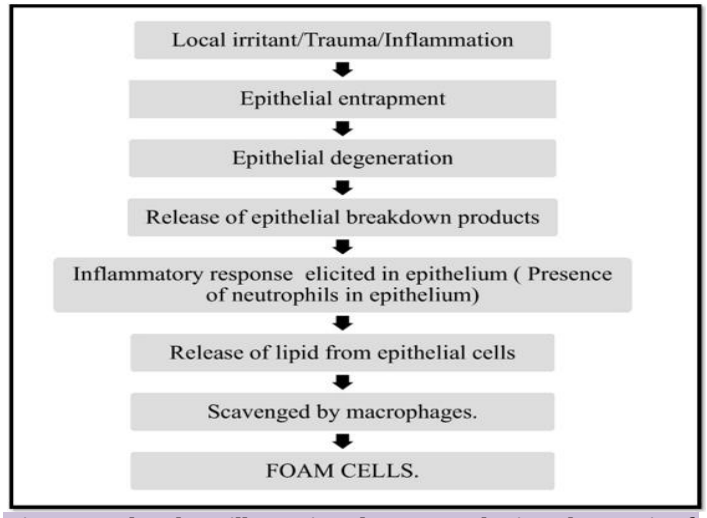

Figure 1: Flowchart illustrating the proposed etiopathogenesis of verruciform xanthoma.

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On gross examination a polypoidal, irregular cauliflower like soft to firm mass measuring 3.5 x 3 cm was received. Cut surface was solid, gray-white with finger like projections.

Microscopic sections revealed hyperplastic stratified squamous epithelium with hyperkeratosis, parakeratosis and papillomatosis. Superficial layer showed presence of neutrophilic infiltrate. Underlying fibrovascular cores showed numerous aggregates of foamy macrophages (xanthoma cells) admixed with lymphoplasmacytic infiltrate [Figure 2B-C]. No definite koilocytosis or dysplasia was seen. Histopathological diagnosis of Verruciform Xanthoma was rendered.

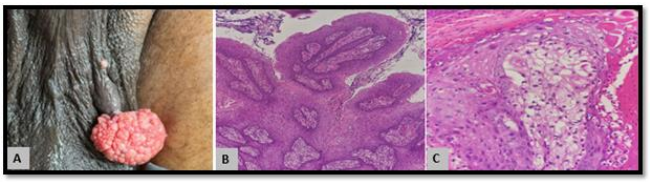

Figure 2: A. Clinical photograph showing a polypoidal verrucous scrotal lesion.B. H&E-stained section (×40) showing papillomatosis, hyperkeratosis, and parakeratosis with elongated rete ridges.C. H&E-stained section (×400) showing neutrophilic infiltrate within the superficial epithelium and numerous foamy macrophages (xanthoma cells) within the underlying fibrovascular cores/connective tissue papillae.

Discussion

Verruciform xanthoma is an uncommon benign reactive lesion.

Clinically it may present as an exophytic, verrucous, or a plaque-like lesion with granular or pebbly surface. The oral cavity is the most commonly affected site (70% of cases) where it can involve keratinized mucosa of palate, gingiva, or alveolar ridge. Rare extraoral cases have also been reported in skin of anogenital region.

The first scrotal verruciform xanthoma was described in 1984 by Al-Nafussi et al.[2] Fukuda and Saito carried out a review of the Japanese literature and found that 81% of verruciform xanthomas in the pubic area were located on the scrotum.[3]

There is no well-defined population incidence rate due to its rarity. A comprehensive review published in 2017 by Stiff et al documented approximately 193 cases of genital verruciform xanthoma in literature; however, additional sporadic cases and small case series have continued to be reported subsequently. Of the 193 cases of genital verruciform xanthoma reported, the scrotum was the most commonly involved site, accounting for nearly 70% (135 cases). The vulva and penis were less frequently involved, with 29 reported cases each, comprising approximately 15% of cases respectively.[2]

Reported genital verruciform xanthomas usually range from a few millimeters to approximately 3 cm in size.[4] The present case measured 3.5 cm in greatest dimension, placing it among the larger lesions described in literature

Genital verruciform xanthoma most commonly affects middle-aged to elderly individuals, particularly males in the fifth to seventh decades of life.

The exact etiopathogenesis of verruciform xanthoma remains uncertain. The most widely accepted hypothesis suggests that it represents a reactive lesion occurring secondary to chronic irritation, inflammation, trauma, or epithelial damage. Degeneration of epithelial cells leads to release of lipid material into the connective tissue, which is subsequently phagocytosed by macrophages, resulting in accumulation of characteristic foamy macrophages (xanthoma cells) within the papillary dermis [Figure 1]. Mostafa et al. suggested that the epithelial hyperplasia in verruciform xanthoma is a result of upward pushing effect by accumulated macrophages towards the epithelium.[5] The foam cells are Periodic Acid Schiff-positive and express CD68 antigen, supporting their histiocytic/macrophage origin.[6]

Clinically, verruciform xanthoma may closely mimic papilloma, verruca vulgaris, condyloma acuminatum, or verrucous carcinoma. Histopathological examination is therefore essential for definitive diagnosis. Microscopically, the lesion is characterized by papillary projections lined by hyperplastic parakeratinized stratified squamous epithelium with relatively uniform elongated rete ridges. The hallmark histopathological feature is the presence of numerous foamy macrophages (xanthoma cells) confined predominantly to the connective tissue papillae, often extending close to the epithelial surface. Neutrophilic exocytosis within the epithelium and subepithelium may also be observed.[1]

Squamous papilloma shows multiple delicate fibrovascular papillary fronds lined by benign stratified squamous epithelium and may demonstrate koilocytic change; however, the characteristic foamy macrophages seen in verruciform xanthoma are absent.

Verruca vulgaris typically demonstrates koilocytic change, coarse hypergranulosis, prominent papillomatosis, and inward curving of rete ridges. Condyloma acuminatum also shows marked papillomatosis and acanthosis with prominent koilocytic atypia involving the superficial squamous epithelium and a well-demarcated bulbous base. Verrucous carcinoma is a well differentiated squamous cell carcinoma with pushing invasive borders showing mitoses and mild cytologic atypia. In contrast, Prominent foamy macrophages are absent in these differential diagnoses.

Verruciform xanthoma is currently considered a reactive inflammatory process, possibly related to chronic irritation, trauma, or epithelial damage. In contrast, verruca vulgaris/condyloma acuminatum, and squamous papilloma are frequently associated with Human Papilloma Virus (HPV) infection, whereas verrucous carcinoma is associated with chronic inflammation, irritation, repeated trauma, and carcinogenic exposure, often requiring wide local excision with careful margin assessment. Although genital verruciform xanthomas may clinically resemble HPV-associated lesions, molecular studies have not consistently demonstrated HPV DNA, favoring a reactive rather than viral pathogenesis.

Complete surgical excision is the treatment of choice. Alternative modalities such as fractionated CO2 laser therapy and topical imiquimod cream have also been used.[2]

The present case is noteworthy because of its relatively large size, scrotal location, and close clinical resemblance to papilloma. Awareness of this entity is important to avoid misdiagnosis as

HPV-related lesions or verrucous malignancy, particularly in elderly patients presenting with genital verrucous growths.

Conclusion

Genital verruciform xanthoma is a rare benign lesion that may clinically simulate HPV-associated lesions and verrucous neoplasms. Recognition of its characteristic histomorphology, particularly the presence of foamy macrophages within fibrovascular cores, is essential to avoid diagnostic pitfalls and to guide appropriate management.

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Conflicts of interest

There are no conflicts of interest.

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